Remarks

The invention, as defined by pending claims 1, 2 and 5 to 20, provides dosage forms which show increased bioavailability of ophthalmologically active compounds by their provision in a dosage form of an ophthalmic treatment liquid which takes the form of a jet or stream of droplets. As explained below, Applicants respectfully submit that the claimed dosage forms are not obvious in light of the cited reference, EP 0 224 352 ("the '352 reference").

Rejection Of Claims 1, 2 and 5 to 20 Under 35 U.S.C. § 103(a) Over EP 0 224 352

The Examiner has rejected claims 1, 2 and 5 to 20 as allegedly being obvious over EP 0 224 352. The Examiner alleged that the dosage form of the '352 reference differs from the claimed dosage form "in the droplet diameter and discharge velocity", and that it allegedly "would have been obvious to a person skilled in the art to determine the droplet size and the velocity of an ophthalmic formulation, considering that the determination of such parameters is considered to be within the skill of the artisan in the absence of evidence to the contrary."

The Examiner further provided:

> One skilled in the art would have been motivated to employ the teachings of the ['352] reference, since it relates to a pharmaceutical dosage in a spray droplet form at the claimed range volume for the treatment of ophthalmic disorders. The ['352] reference makes clear that the drug has been delivered at the proper dosage, and the intended treatment has been accomplished. The determination of droplet size is considered to be within the skill of the artisan in the absence of evidence to the contrary.

While the Examiner has considered our previously submitted data and also many relevant and reasonable arguments distinguishing the prior art, Applicants again respectfully disagree with the Examiner's characterization of the '352 reference.

<u>The '352 Reference Does Not Disclose A Stream or Specified Droplet Velocity And/Or Size</u>

The '352 reference discloses "electrodynamic spraying" that causes the "formulation to atomise as a spray of electrically charged droplets" ('352 Application, page 2, lines 25 – 32). Further, the '352

Application provides that "[t]his process provides a particularly even, accurately targetted, coating of the eye with the formulation" (Id. at lines 35 – 37).

As previously presented in Applicants' Responses to the PTO, the '352 reference does not disclose a stream or droplet velocity, but rather focuses on a "fine spray of electrically charged particles". Also, the present invention is clearly distinguishable and non-obvious based on particular droplet size to maximize its use in treating ophthalmic disorders via narrowly targetted areas within the patient's eye. The present invention does not require the "coating" aspect of the '352 reference, as the present formulation can be specifically targetted to various sub-structures of the eye. Further, the '352 reference does not address the ability of the present invention to defeat a user's blinking reflex by employing the novel stream and specified droplet size and delivery velocity, which all clearly differentiate the invention from the '352 reference. For example, see page 1, column 2, paragraph 008 of Applicants' published application("[T]he entire volume can be delivered to the chosen site on the eye before the patient blinks to disperse the received fluid"). Accordingly, Applicants submit that the present invention is non-obvious in light of the '352 reference's teachings.

The '352 Reference Teaches Away From Aqueous Formulations

The '352 reference explicitly provides:

> [T]he formulation may not be predominantly aqueous as it has been found that aqueous formulations do not undergo electrodynamic spraying satisfactorily due to their high conductivity. Preferably, the amount of water, if any is present, comprises not more than about 20% by weight of the total diluent, and preferably less than 10% by weight. ('352 Application, page 4, lines 1 – 6 (emphasis added)).

Clearly, this passage from the '352 references actually teaches away from using any formulation that is aqueous, due to incompatibility with the electrodynamic atomisation required in the '352 reference, as noted by the above-quoted passage from the '352 reference.

In contrast, the present invention expressly provides for aqueous formulations, and this aspect of the invention is clearly reflected in the invention. For example, see page 4, column 1, paragraph 0044 of the published application ("Ophthalmic treatment liquids that may be used with the invention may be

aqueous…"). Also refer to page 4, column 2, paragraph 0063 ("The compounds may be formulated as aqueous or non-aqueous (e.g., oil) solutions or suspensions").

Accordingly, since the '352 reference explicitly teaches away from the use of aqueous formulations, then the present invention is clearly non-obvious by providing for aqueous formulations that are prohibited by the '352 reference. Such clear language within the '352 reference negates any allegation of obviousness regarding the present invention.

Conclusion

Applicants respectfully submit that the above arguments demonstrate non-obviousness of the current invention in view of the '352 reference. Withdrawal of the rejection under 35 USC § 103(a) is respectfully requested.

If any extensions of time are necessary for the submission of this response, then Applicants respectfully petition for such extension(s), and request that such fees and any other fees be charged to deposit account 500329.

Respectfully submitted,

Date: **December 12, 2006**

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